Arntzen et al. teaches a method for making a transgenic tobacco, tomato or potato that expresses HBsAg.

Arntzen et al. recognize that not all antigens would cause an immune response if ingested.

Arntzen et al. says in column 15 beginning at line 27,

> "The vaccines are conventionally administered parenterally, by injection, for example either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, ***in some cases***, oral formuilations or aerosols." (Emphasis added).

While Arntzen et al. suggest that tomato juice containing HBsAg might be used as a vaccine, in fact Arntzen provides no supporting data showing any immune response whatsoever to tomato juice or any other plant containing HBsAg. To the extent that Arntzen teaches that tomato juice or any other plant material containing HBsAg can be used as a vaccine, it is an inoperative reference since there is no teaching or suggestion as to how that might be done. ***Simply ingesting the plant material, as suggested by Arntzen et al., does not confer immunity***.

There is good reason for Arntzen's omission of data showing immune response to HBsAg by ingesting food material containing it, since prior to the present invention, in fact, there was little if any immune response whatsoever to HBsAg in orally ingested tomato juice or any other plant expressing HBsAg. The response, if any, is clearly insufficient for that purpose.

Reference to the examples in the present specification clearly illustrates that priming of the subject of the immunization is required by either pre-vaccination or the use of an effective adjuvant. Arntzen et al. suggests neither. Arntzen et al. doesn't suggest an adjuvant for any purpose whatsoever and certainly does not suggest a combination with an adjuvant that permits the obtaining of a high immune response to orally administered HBsAg as required by the present claims.

Arntzen et al. therefore does not disclose or suggest the presently claimed invention.

Claims 1-3 and 20 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Arntzen et al. above or U.S. Patent 5,935,570 to Koprowski et al. in view of Stites et al. Basic and Clinical Immunology, pp 723-741.

The rejection is improper and should be withdrawn.

Arntzen does not disclose or suggest the present invention, as previously discussed. Arntzen's suggestion of simple ingestion of plant material expressing HBsAg does not give a sufficient immune response to be considered protective. Arntzen discloses or suggests no way in which a high immune response could be orally obtained. ***In any case there is certainly no suggestion of the enhanced immune response to HBsAg in orally administered plant material as provided by the method presently claimed.***

The Examiner states that Koprowski "teaches methods of making a transgenic plant containing a viral antigen which is fed to an animal or human to elicit an immune response." The Examiner's statement is inaccurate. Koprowski at al. does not teach or suggest any method for making a transgenic plant but teaches a microorganism expressing a bioactive compound,

e.g., an immunogenic rabies polypeptide. The microorganism may then be used to infect a plant as a parasite but does not alter the genetic character or expression of the plant.

Kaprowski et al. suggest that their method has wide application, e.g., for treatment of viral infections, bacterial infections, fungal infections, protozoan infections, diabetes, immune disorders, cancer and heart disease. Kaprowski et al. more specifically suggest that their method could be used for mucosal pathogens, e.g. rabies, respiratory syncytial virus, cholera, typhoid fever, herpes simplex types I and II, tuberculosis, pathogenic pneumococci, human immunodeficiency virus-1 (HIV-1) and human immunodeficiency virus-2 (HIV-2).

The only specific example given is for rabies. There is no enablement for the other suggested applications. If the disclosure actually enabled everything suggested, oral vaccines effective against AIDS, cancer, and herpes, among many others, would be made available simply by following the teachings of the Kaprowski et al patent. It is well known that this is not the case.

Kaprowski et al. certainly does not enable or even reasonably suggest application for orally raising an immune response to hepatitis b surface antigen. The suggestion that an adjuvant be used is a gratuitous statement applied across the entire non-enabled spectrum of the Kaprowski et al. disclosure. There is no suggestion of any specific adjuvant that would have such an effect for purposes of enablement and in fact there is no suggestion that any adjuvant would have any effect whatsoever upon oral immune response to hepatitis B surface antigen.

Stites et al. adds nothing to cure the inadequate teachings and suggestions of Arntzen et al. and Kaprowski et al. Stites does not suggest anything whatsoever concerning hepatitis B and

certainly suggests nothing suggesting that HBsAg would orally raise a highly effective immune response in the presence of a suitable adjuvant as presently claimed.

Claims 4-19 have been rejected under 35 U.S.C. 103 over Arntzen et al. in view of Stites et al., and Kaprowski et al.

The rejection should be withdrawn.

None of the references, alone or in combination, enable the raising of an oral immune response to HBsAg in plants and certainly do not suggest that an enhanced oral response to HBsAg could be obtained when the oral administration was conducted after a primary immunization. In any case the rejection is an applicable to the claims, as amended, since the claims are not now directed to ingesting plant material containing HBsAg after a primary immunization.

It is requested that the rejections over copending application 09/418,177 be temporarily held in abeyance since application 09/418,177 is being allowed to go abandon by failure to respond. The rejections will thus be moot.

Claims 3-14 and 16 have been rejected on the grounds that they conflict with claims of Application No. 09/464,414.

It is requested that this rejection be withdrawn. The claims of 09/464,414 claim subject matter where an animal is made immunoreceptive by immunization prior to feeding plant material containing HBsAg. The claims as amended no longer claim subject matter where an animal is made immunoreceptive by immunization prior to feeding plant material containing HBsAg. The present claims are restricted to the use of an adjuvant. The claims of 09/464,414

do not require adjuvant. The present claims and the claims of 09/464,414 thus no longer overlap and are not obvious in view of each other.

Claims 1-2 of the present application have been rejected as being in conflict with Claims 2 and 14 of Application No. 09/464,416.

The rejection is not understood, since according to our records, there are only 12 claims in 09/464,416 thus a rejection in view of Claim 14 is not possible. It is assumed that the rejection should be in view of Claims 2 and 4. If this assumption is not correct, **clarification in a non-final action is requested.**

In view of the significant amendments to Claim 1 and cancellation of Claim 2, there is no longer any conflict.

The rejections of the claims 35 U.S.C. 101 for claiming the same inventions as copending applications are rendered moot for the reasons given above removing conflict of claims.

Claims 19-20 have been rejected for obviousness type double patenting over U.S. Patent 5,914,123.

This rejection has been rendered moot by cancellation of Claims 19-20.

Claims 1-20 have been rejected for obviousness type double patenting in view of copending application 09/464,416.

A terminal disclaimer is enclosed overcoming this rejection.

Claims 1-17 have been rejected for obviousness type double patenting over copending application 09/464,414.

It is requested that this rejection be withdrawn. The claims of 09/464,414 claim subject matter where an animal is made immunoreceptive by immunization prior to feeding plant material containing HBsAg. The claims as amended no longer claim subject matter where an animal is made immunoreceptive by immunization prior to feeding plant material containing HBsAg. The present claims are restricted to the use of an adjuvant. The claims of 09/464,414 do not require adjuvant. The present claims and the claims of 09/464,414 thus no longer overlap and are not obvious in view of each other.

In view of the foregoing amendments and remarks, it is courteously requested that all rejections be withdrawn and all claims be allowed.

Respectfully submitted,

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